Non-negative matrix factorization of hippocampal-cortical resting state functional connectivity

Raihaan Patel[1,2], Anthony Chen[1,3], Sejal Patel[1,4,5], M. Mallar Chakravarty[1,2,6]

[1]Cerebral Imaging Centre, Douglas Mental Health University Institute, Verdun, Canada; [2]Department of Biological and Biomedical Engineering, McGill University, Montreal, Canada; [3]Department of Neuroscience, McGill University, Montreal, Canada; [4]Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, Canada; [5]Institute of Medical Science, University of Toronto, Toronto, Canada; [6]Department of Psychiatry, McGill University, Montreal, Canada

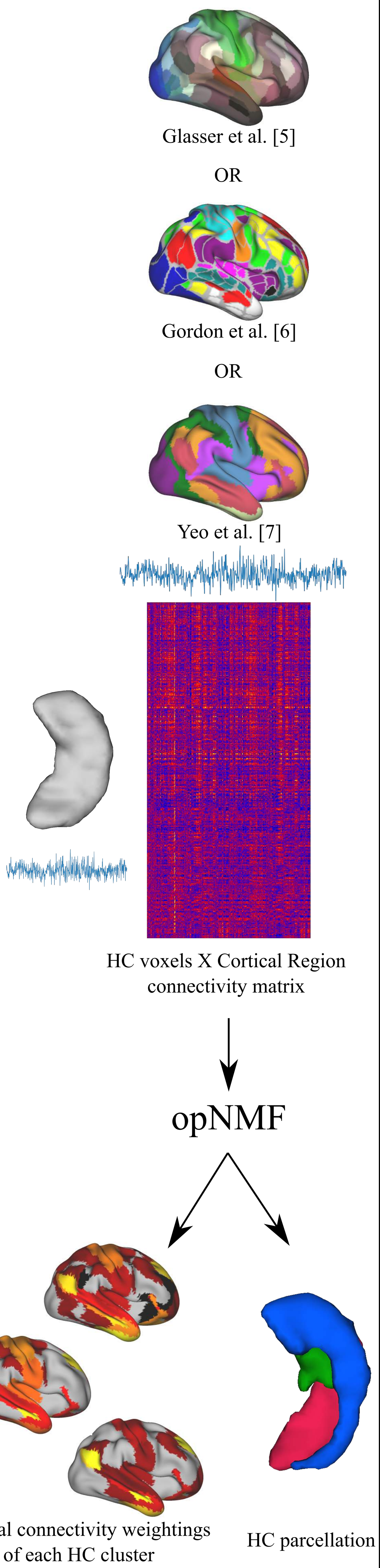
Introduction

The hippocampus (HC) is a brain structure linked with learning and memory, and known to have widespread cortical connectivity. Most works assess the HC at a gross spatial scale, as a single structure or based on subfields. Here we use a data-driven methodology to assess spatial patterns of HC-cortical resting state functional connectivity (RSFC).

Methods

Image Processing: We obtained extensively processed resting state frmi ($2mm^3$) data from 100 unrelated subjects of the Human Connectome Project [1,2] and performed mean grayordinate time series regression [3] on top of the ICA-FIX preprocessing [4]. Using three different cortical atlases [5-7], we averaged time series within each cortical region, then computed correlations between each HC voxel and each cortical region to obtain HC-cortical network matrices. Correlations were transformed using Fisher z-transform.

Parcellation: We used orthogonal projective non-negative matrix factorization (opNMF) [8-11] to parcellate the hippocampus based on HC-cortical RSFC. Given an HC-cortical network matrix, opNMF outputs HC clusters with similar RSFC patterns, as well as weightings for each cortical region describing connectivity of each HC cluster. opNMF was performed on group average network matrices, and performed separately for left and right HC.



Stability: We analyzed stability and accuracy of 2 - 10 component decompositions. For stability, we iteratively split data into two groups and performed opNMF on the average network matrix of each group. We then correlate the output component score patterns of each hippocampal voxel to obtain a measure of similarity of the output spatial patterns across the two groups. We repeated this 10 times for each granularity. We also tracked the gradient of the reconstruction error to measure accuracy vs. complexity.

Results

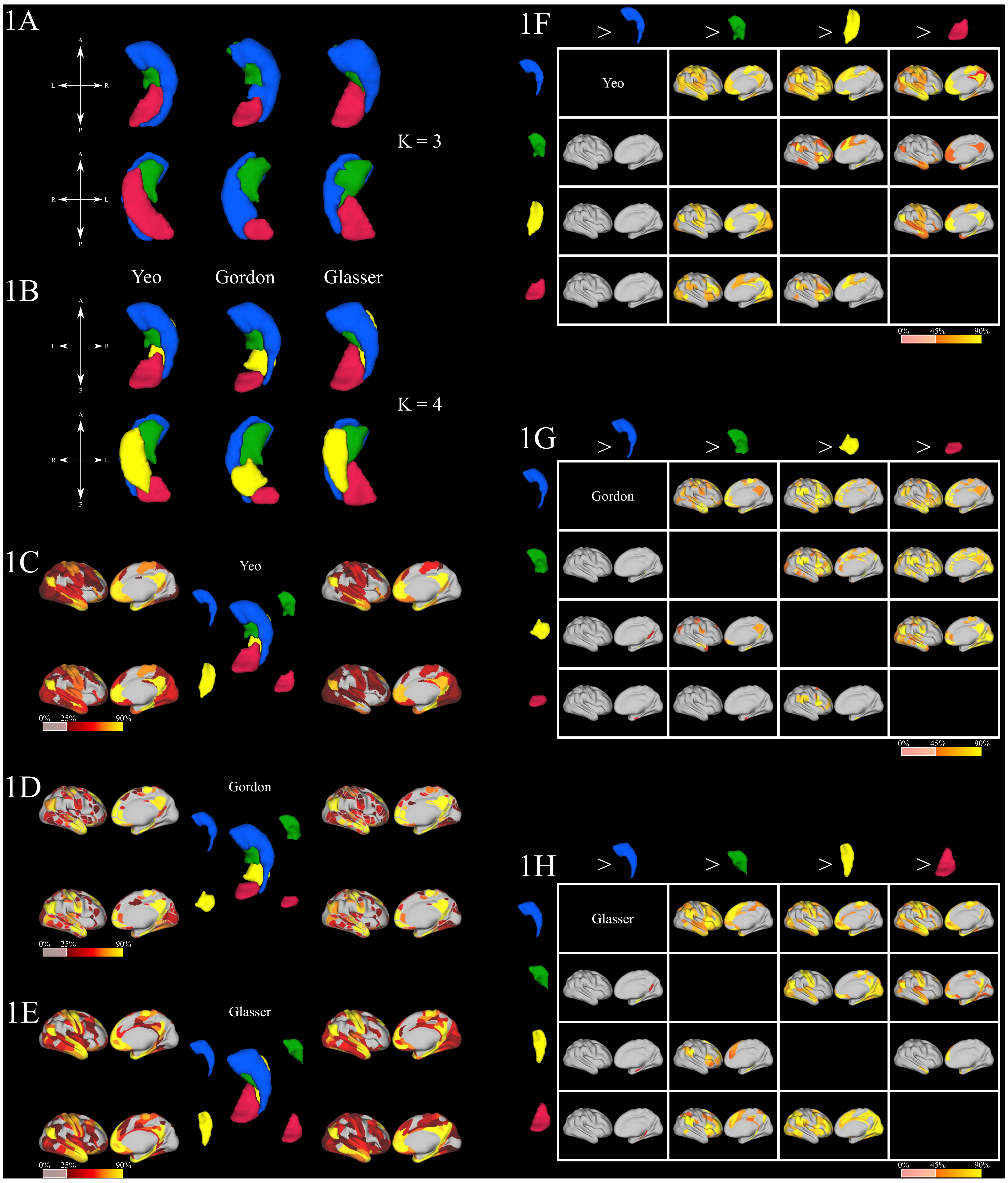


Figure 1. Output hippocampal clusters and cortical connectivity patterns. A-B: visual representations of the 3(1A) and 4(1B) cluster solutions (top row: superior view, bottom row: inferior view). Separation along the anterior-posterior axis is identified (blue/green vs yellow/red). In the head of the hippocampus, a medial-lateral separation is consistent (blue vs green). C-E: maps of the weightings of each cortical region for each of the 4 cluster solutions. In these maps, high values relate to increased connectivity to a given HC cluster. F-H: Contrast maps obtained by cortical weights of a given component from another, for each pairwise combination of clusters, for each of the 4 cluster solutions. These maps show which preferential cortical connectivity of a given cluster in comparison to another. HC 3D renderings obtained using Mango[13]. Cortical figures obtained using HCP's Connectome Workbench[14]

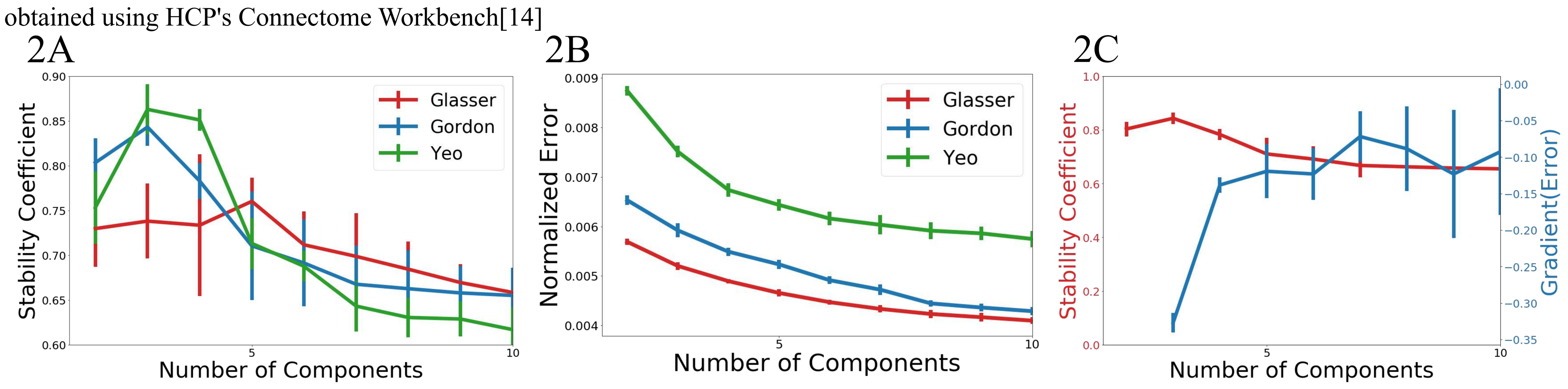


Figure 2. Stability and reconstruction error properties for the three inputs used. Figure 2A plots the stability coefficient for granularities 2-10, for opNMF of the right HC and each of the input atlases. Figure 2B plots the normalized reconstruction error for opNMF of the right HC with each input across granularities. Based on this, we selected HC clusters obtained using the Gordon atlas for further study, as a balance between normalized error and stability. Figure 2C plots the stability coefficient versus the error gradient for opNMF of the right HC using the Gordon atlas. A large gain in error is shown when moving from 3 to 4 components, and error is relatively stable after. Thus, the 4 component solution was selected to investigate cortical patterns.

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Conclusion

We used opNMF to identify clusters showing consistent longitudinal and lateral-medial separation based on HC-cortical RSFC. Many HC analyses often employ subfield definitions which lack longitudinal differentiation despite contrary evidence [12] which this work supports. In addition to this, we also show that functional separation on the lateral-medial axis can be found in the hippocampus. Together, these results support the use of multimodal information to define boundaries.

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